## AMENDMENTS TO THE CLAIMS

Docket No.: 3893-0232PUS2

 $1.\ (Original)\ A\ method\ of\ preparing\ a\ compound\ of\ general\ structure\ Va,\ Vb,\ VIIIa,\ VIIIb,$ 

XIVa, XIVb, XVIa, XVIb, or XX respectively,

$$R_2O$$

OR<sub>1</sub>
 $R_1O$ 

OR<sub>2</sub>
 $R_1O$ 

OR<sub>2</sub>
 $R_1O$ 

OR<sub>1</sub>

OR<sub>2</sub>

OR<sub>1</sub>

OR<sub>1</sub>

OR<sub>1</sub>

OR<sub>1</sub>

OR<sub>1</sub>

OR<sub>1</sub>

OR<sub>1</sub>

wherein  $R_1$  and  $R_2$  are the same or different and represent hydrogen or a hydroxy protecting group, and wherein  $R_5$  represents hydrogen or a hydroxy protecting group;

the method comprising reacting a compound of general structure IIIa, IIIb, VIa, VIb, XIIIa,

XIIIb, XVa, or XVb, or IXX respectively,

$$R_2O$$
 $OR_1$ 
 $R_1O$ 
 $OR_2$ 
 $R_2O$ 
 $OR_1$ 
 $R_2O$ 
 $OR_2$ 
 $OR_2$ 
 $OR_2$ 
 $OR_2$ 
 $OR_2$ 
 $OR_2$ 
 $OR_2$ 
 $OR_3$ 
 $OR_4$ 
 $OR_4$ 
 $OR_5$ 
 $OR_5$ 
 $OR_6$ 
 $OR_7$ 
 $OR_7$ 
 $OR_8$ 
 $OR_8$ 
 $OR_9$ 
 $OR_9$ 

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wherein R<sub>1</sub>, R<sub>2</sub>, and R<sub>5</sub> are as defined above; with a phosphonate of general structure VII,

IXX

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wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, aralkyl, aralkyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected form the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkynyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy, in the presence of a base.

2. (Original) A method according to claim 1 of preparing a compound of general structure Va,

wherein  $R_1$  and  $R_2$  are the same or different and each represent hydrogen or a hydroxy protecting group,

the method comprising reacting a compound of general structure IIIa,

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wherein R1 and R2 are as defined above,

with a phosphonate of general structure VII,

wherein R<sub>3</sub> and R<sub>4</sub> are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected form the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy, in the presence of a base.

3. (Original) A method according to claim 1 of preparing a compound of general structure Vb,

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wherein  $R_1$  and  $R_2$  are the same or different and each represent hydrogen or a hydroxy protecting group,

the method comprising reacting a compound of general structure IIIb,

wherein R1 and R2 are as defined above,

with a phosphonate of general structure VII,

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wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, aralkynyl, aralkynyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected form the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy, in the presence of a base.

 (Original) A method according to claim 1 of preparing a compound of general structure VIIIa or VIIIb respectively.

wherein  $R_1$  and  $R_2$  are the same or different and each represent hydrogen or a hydroxy protecting group,

the method comprising reacting a compound of general structure VIa or VIb respectively,

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wherein  $R_1$  and  $R_2$  are as defined above, with a phosphonate of general structure VII,

wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, aralkynyl, aralkynyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected form the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkynyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy, in the presence of a base.

5. (Original) A method according to claim 1 of preparing a compound of general structure XIVa,

wherein R<sub>1</sub> represents hydrogen or a hydroxy protecting group,

the method comprising reacting a compound of general structure XIIIa,

wherein R<sub>1</sub> is as defined above,

with a phosphonate of general structure VII,

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wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, aralkynyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected form the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy, in the presence of a base.

6. (Original) A method according to claim 1 of preparing a compound of general structure XIVb.

wherein  $R_1$  represents hydrogen or a hydroxy protecting group, the method comprising reacting a compound of general structure XIIIb,

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wherein R1 is as defined above,

with a phosphonate of general structure VII,

wherein R<sub>3</sub> and R<sub>4</sub> are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected form the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy, in the presence of a base.

 (Original) A method according to claim 1 of preparing a compound of general structure XVIa or XVIb respectively,

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wherein R<sub>1</sub> represents hydrogen or a hydroxy protecting group,

the method comprising reacting a compound of general structure XVa or XVb respectively,

wherein R1 is as defined above,

with a phosphonate of general structure VII,

wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, aralkynyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected form the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy, in the presence of a base.

## 8. (Original) A method according to claim 1 of preparing a compound of general structure XX,

wherein R5 represents hydrogen or a hydroxy protecting group,

the method comprising reacting a compound of general structure IXX,

wherein Rs is as defined above.

with a phosphonate of general structure VII,

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wherein R<sub>3</sub> and R<sub>4</sub> are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected form the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy, in the presence of a base.

- (Previously Presented) A method of preparing calcipotriol or calcipotriol monohydrate, the method comprising the method according to claim 1 or 2.
- 10. (Original) A method for producing calcipotriol or calcipotriol monohydrate according to claim 9, the method comprising the steps of:
- (i) reacting a compound of general structure IIIa,

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wherein  $R_1$  and  $R_2$  are the same or different and represent hydrogen or a hydroxy protecting group,

with a phosphonate of general structure VII.

wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected form the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkynyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy, in the presence of a base,

to give a compound of general structure Va,

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wherein R1 and R2 are as defined above;

(ii) reducing the compound of general structure Va with a suitable reducing agent,

to give a compound of general structure IXa or a mixture of compounds of general structure IXa and IXb.

wherein R1 and R2 are as defined above;

(iii) optionally separating the compound of general structure IXa from the mixture of compounds of general structure IXa and IXb;

(iv) photoisomerising the compound of general structure IXa to the compound of general structure Xa.

wherein R<sub>1</sub> and R<sub>2</sub> are as defined above;

- (v) when  $R_1$  and/or  $R_2$  are not hydrogen, removing the hydroxy protecting group(s)  $R_1$  and/or  $R_2$  of the compound of general structure Xa to generate calcipotriol; and
- (vi) optionally crystallising the calcipotriol from a mixture of an organic solvent and water to give calcipotriol monohydrate.
- 11. (Original) A method for producing calcipotriol or calcipotriol monohydrate according to claim 9, the method comprising the steps of:
- (i) reacting a compound of general structure IIIb,

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wherein  $R_1$  and  $R_2$  are the same or different and represent hydrogen or a hydroxy protecting group,

with a phosphonate of general structure VII,

wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, aralkyl, aralkyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected form the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkynyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy, in the presence of a base,

to give a compound of general structure Vb,

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wherein R1 and R2 are as defined above;

(ii) reducing the compound of general structure Vb with a suitable reducing agent, to give a compound of general structure Xa or a mixture of compounds of general structure Xa and Xb,

wherein R1 and R2 are as defined above;

(iii) optionally separating the compound of general structure Xa from the mixture of compounds of general structure Xa and Xb;

(iv) when  $R_1$  and/or  $R_2$  are not hydrogen, removing the hydroxy protecting group(s)  $R_1$  and/or  $R_2$  of the compound of general structure Xa to generate calcipotriol; and

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- (v) optionally crystallising the calcipotriol from a mixture of an organic solvent and water to give calcipotriol monohydrate.
- 12. (Original) A method for producing calcipotriol or calcipotriol monohydrate according to claim 9, the method comprising the steps of:
- (i) reacting a compound of general structure VIa and/or VIb,

wherein  $R_1$  and  $R_2$  are the same or different and represent hydrogen or a hydroxy protecting group,

with a phosphonate of general structure VII,

wherein R3 and R4 are the same or different and represent alkyl, haloalkyl, hydroxyalkyl,

alkenyl, aralkyl, aralkyl, aralkynyl, or aryl, each being optionally substituted with one

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or more substituents selected form the group consisting of alkyl, aralkyl, cycloalkyl,

cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy,

in the presence of a base,

to give a compound of general structure VIIIa and/or VIIIb,

wherein R1 and R2 are as defined above;

(ii) heating the compounds of general structure VIIIa and/or VIIIb above 60°C in the presence of a base.

to give a compound of general structure Va.

wherein R1 and R2 are as defined above;

(iii) reducing the compound of general structure Va with a suitable reducing agent,

to give a compound of general structure IXa or a mixture of compounds of general structure IXa and IXb.

wherein R1 and R2 are as defined above;

(iv) optionally separating the compound of general structure IXa from the mixture of compounds of general structure IXa and IXb;

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(v) photoisomerising the compound of general structure IXa to the compound of general structure Xa,

wherein R1 and R2 are as defined above;

- (vi) when  $R_1$  and/or  $R_2$  are not hydrogen, removing the hydroxy protecting group(s)  $R_1$  and/or  $R_2$  of the compound of general structure Xa to generate calcipotriol; and
- (vii) optionally crystallising the calcipotriol from a mixture of an organic solvent and water to give calcipotriol monohydrate.
- 13. (Original) A method for producing calcipotriol or calcipotriol monohydrate according to claim 9, the method comprising the steps of:
- (i) reacting a compound of general structure VIa and/or VIb,

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wherein  $R_1$  and  $R_2$  are the same or different and represent hydrogen or a hydroxy protecting group,

with a phosphonate of general structure VII,

wherein R<sub>3</sub> and R<sub>4</sub> are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected form the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy, in the presence of a base,

to give a compound of general structure VIIIa and/or VIIIb,

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wherein R1 and R2 are as defined above;

(ii) reducing the compounds of general structure VIIIa and/or VIIIb, with a suitable reducing agent in an inert solvent,

to give compounds of general structure XIaa and/or XIba, or a mixture of compounds of general structure XIaa and/or XIba and XIab and/or XIbb,

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wherein R1 and R2 are as defined above;

- (iii) optionally separating the compounds of general structure XIaa and/or XIba from the reaction mixture;
- (iv) heating the compounds of general structure XIaa and/or XIba above  $60^{\circ}\text{C}$  in the presence of a base,

to give a compound of general structure IXa,

wherein R1 and R2 are as defined above;

- (v) optionally separating the compound of general IXa from the reaction mixture;
- (vi) photoisomerising the compound of general structure IXa to the compound of general structure Xa.

wherein R1 and R2 are as defined above;

(vii) when  $R_1$  and/or  $R_2$  are not hydrogen, removing the hydroxy protecting group(s)  $R_1$  and/or  $R_2$  of the compound of general structure  $X_2$  to generate calcipotriol; and

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(viii) optionally crystallising the calcipotriol from a mixture of an organic solvent and water to give calcipotriol monohydrate;

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wherein steps (vi) and (vii) may be in reversed order.

14. (Original) A method for producing calcipotriol or calcipotriol monohydrate according to claim 9, the method comprising the steps of:

(i) reacting a compound of general structure XIIIa,

wherein R<sub>1</sub> represents hydrogen or a hydroxy protecting group, with a phosphonate of general structure VII.

wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkynyl, or aryl, each being optionally substituted with one

or more substituents selected form the group consisting of alkyl, aralkyl, cycloalkyl,

cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkynyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy,

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in the presence of a base,

to give a compound of general structure XIVa,

wherein R1 is as defined above;

(ii) hydroxylating the compound of general structure XIVa with suitable hydroxylating agent, to give a compound of general structure Va,

represent a hydroxy protecting group;

wherein R<sub>1</sub> represents hydrogen or a hydroxy protecting group and R<sub>2</sub> is hydrogen;

- (iii) optionally reacting the compound of general structure Va, wherein  $R_1$  represents hydrogen or a hydroxy protecting group and  $R_2$  is hydrogen with a suitable protecting agent, to give a compound of general structure Va, wherein  $R_1$  and  $R_2$  are the same or different and
- (iv) reducing the compound of general structure Va with a suitable reducing agent,
  to give a compound of general structure IXa or a mixture of compounds of general structure IXa
  and IXb,

wherein R1 and R2 are as defined above;

- (v) optionally separating the compound of general structure IXa from the mixture of compounds of general structure IXa and IXb;
- (vi) photoisomerising the compound of general structure IXa to a compound of general structure Xa,

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wherein R<sub>I</sub> and R<sub>2</sub> are as defined above;

- (vii) when  $R_1$  and/or  $R_2$  are not hydrogen, removing the hydroxy protecting group(s)  $R_1$  and/or  $R_2$  of the compound of general structure  $X_2$  to generate calcipotriol; and
- (viii) optionally crystallising the calcipotriol from a mixture of an organic solvent and water to give calcipotriol monohydrate.
- 15. (Original) A method for producing calcipotriol or calcipotriol monohydrate according to claim 9, the method comprising the steps of:
- (i) reacting a compound of general structure XIIIb,

wherein R<sub>1</sub> represents hydrogen or a hydroxy protecting group, with a phosphonate of general structure VII,

wherein R<sub>3</sub> and R<sub>4</sub> are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected form the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy, in the presence of a base.

to give a compound of general structure XIVb,

wherein R1 is as defined above;

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(ii) photoisomerising the compound of general structure XIVb to a compound of general structure XIVa.

wherein R<sub>1</sub> is as defined above;

(iii) hydroxylating the compound of general structure XIVa with suitable hydroxylating agent, to give a compound of general structure Va,

wherein R<sub>1</sub> represents hydrogen or a hydroxy protecting group and R<sub>2</sub> is hydrogen;

(iv) optionally reacting the compound of general structure Va, wherein R<sub>1</sub> represents hydrogen or a hydroxy protecting group and R<sub>2</sub> is hydrogen with a suitable protecting agent to give a

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compound of general structure Va, wherein  $R_1$  and  $R_2$  are the same or different and represent a hydroxy protecting group;

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(v) reducing the compound of general structure Va with a suitable reducing agent,

to give a compound of general structure IXa or a mixture of compounds of general structure IXa and IXb.

wherein R<sub>1</sub> and R<sub>2</sub> are as defined above;

- (vi) optionally separating the compound of general structure IXa from the mixture of compounds of general structure IXa and IXb;
- (vii) photoisomerising the compound of general structure IXa to the compound of general structure Xa.

wherein R1 and R2 are as defined above;

- $\label{eq:continuous} \mbox{(viii) when $R_1$ and/or $R_2$ are not hydrogen, removing the hydroxy protecting group(s) $R_1$ and/or $R_2$ of the compound of general structure Xa to generate calcipotriol; and $R_2$ of the compound of general structure is a second of the compound of general structure and the second of the compound of general structure is a second of the compound of general structure is a second of the compound of general structure is a second of the compound of general structure. \\$
- (ix) optionally crystallising the calcipotriol from a mixture of an organic solvent and water to give calcipotriol monohydrate.
- 16. (Original) A method for producing calcipotriol or calcipotriol monohydrate according to claim 9, the method comprising the steps of:
- (i) reacting a compound of general structure XVa and/or XVb,

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wherein R<sub>1</sub> represents a hydrogen or a hydroxy protecting group. with a phosphonate of general structure VII,

wherein R3 and R4 are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected form the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy, in the presence of a base,

to give a compound of general structure XVIa and/or XVIb.

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wherein R1 is as defined above;

 (ii) heating the compounds of general structure XVIa and/or XVIb above 60°C in the presence of a base,

to give a compound of general structure XIVa,

wherein R1 is as defined above;

(iii) hydroxylating the compound of general structure XIVa with suitable hydroxylating agent, to give a compound of general structure Va.

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wherein R1 represents hydrogen or a hydroxy protecting group and R2 is hydrogen;

- (iv) optionally reacting the compound of general structure Va, wherein  $R_1$  represents hydrogen or a hydroxy protecting group and  $R_2$  is hydrogen with a suitable protecting agent,
- to give a compound of general structure Va, wherein  $R_1$  and  $R_2$  are the same or different and represent a hydroxy protecting group;
- (v) reducing the compound of general structure Va with a suitable reducing agent,
   to give a compound of general structure IXa or a mixture of compounds of general structure IXa
   and IXb,

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wherein R1 and R2 are as defined above;

(vi) optionally separating the compound of general structure IXa from the mixture of compounds of general structure IXa and IXb;

(vii) photoisomerising the compound of general structure IXa to the compound of general structure Xa.

wherein R1 and R2 are as defined above;

(viii) when  $R_1$  and/or  $R_2$  are not hydrogen, removing the hydroxy protecting group(s)  $R_1$  and/or  $R_2$  of the compound of general structure Xa to generate calcipotriol; and

(ix) optionally crystallising the calcipotriol from a mixture of an organic solvent and water to give calcipotriol monohydrate.

17. (Original) A method for producing calcipotriol or calcipotriol monohydrate according to claim 9, the method comprising the steps of:

(i) reacting a compound of general structure IXX,

wherein R<sub>5</sub> represents hydrogen or a hydroxy protecting group, with a phosphonate of general structure VII,

wherein R<sub>3</sub> and R<sub>4</sub> are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected form the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy, in the presence of a base,

to give a compound of general structure XX,

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wherein R5 is as defined above;

(ii) reducing the compound of general structure XX with a suitable reducing agent, to give a compound of general structure XXIa or a mixture of compounds of general structure

XXIa and XXIb.

wherein R5 is as defined above and R6 is hydrogen;

- (iii) optionally separating the compound of general structure XXIa from the mixture of compounds of general structure XXIa and XXIb;
- (iv) protecting the allylic hydroxy group of the compound of general structure XXIa with a suitable hydroxy protecting reagent,
- to give a compound of general structure XXIa, wherein  $R_6$  is a hydroxy protecting group and  $R_5$  is as defined above:
- (v) when  $R_5$  is not hydrogen, removing the hydroxy protecting group  $R_5$  of the compound of general structure XXIa to give a compound of general structure XXIa, wherein  $R_5$  is hydrogen;

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(vi) oxidising the hydroxy group of the compound of general structure XXIa with a suitable oxidising agent to give a compound of general structure XXII,

wherein R6 is as defined above;

(vii) coupling of the compound of general structure XXII with a Wittig reagent XXIIIa or a Wittig Horner reagent XXIIIb,

wherein  $R_1$  and  $R_2$  represent a hydrogen or a hydroxy protecting group, and wherein  $R_3$  and  $R_4$  are as defined above;

in the presence of a base,

to give a compound of general structure XXIVa,

wherein  $R_1$  and  $R_2$  are the same or different and represent hydrogen or a hydroxy protecting group, and wherein  $R_6$  is as defined above;

- (viii) when  $R_6$  is not hydrogen, removing the hydroxy protecting group  $R_6$  of the compound of general structure XXIVa;
- (ix) optionally separating the compound of general structure XXIVa;
- (x) when R<sub>1</sub> and R<sub>2</sub> are not hydrogen, removing the hydroxy protecting group(s) R<sub>1</sub> and R<sub>2</sub> of the compound of general structure XXIVa to generate calcipotriol;

and

- (xi) optionally crystallising the calcipotriol from a mixture of an organic solvent and water to give calcipotriol monohydrate.
- 18. (Cancelled)
- 19. (Currently Amended) The method according to claim 1-o≠-2, wherein R<sub>3</sub> and R<sub>4</sub> are methyl or ethyl.

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20. (Previously Presente) The method according to claim 1, wherein  $R_1$  and  $R_2$  represent

hydrogen or alkylsilyl.

21. (Currently Amended) The method according to claim 1-or 2, wherein R1 and R2 represent

hydrogen or tert-butyldimethylsilyl.

22. (Cancelled)

23. (Currently Amended) The method according to claim 1-or 2, wherein the reaction with the

phosphonate of general structure VII is carried out under phase-transfer conditions.

24. (Currently Amended) The method according to claim 1-or-2, wherein the reaction with the

phosphonate of general structure VII is carried out under phase-transfer conditions in a mixture

of toluene or xylene and water with a tetraalkylammonium halide or a tetraalkylammonium

hydrogensulfate as the phase transfer catalyst and with an alkalimetal hydroxide and/or a

tetraalkylammoniumhydroxide as the base.

25. (Previously Presented) The method according to claim 1, wherein the reaction with the

phosphonate of general structure VII is carried out at a temperature between 10°C-50°C.

26. - 29. (Cancelled)

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30. (Original) A compound of general structure VII,

wherein R<sub>3</sub> and R<sub>4</sub> are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected form the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy, provided that that the compound is not (2-cyclopropyl-2-oxoethyl)phosphonic acid diethyl ester.

31. - 44. (Cancelled)

47 ADM/mao